Salivary Duct Carcinoma: A Single-Institution, 20-Year Review of 75 Cases

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INTRODUCTION

Salivary duct carcinoma is a rare, aggressive malignancy of the salivary glands, with many patients dying within the first year after presentation. Due to its rare nature, clinical data is limited, and there are only a few clinical studies that comprise more than 50 patients. We reviewed our institution's experience with this disease over a 20-year period.

DESIGN AND METHODS

Design: Retrospective cohort study
Setting: Multi-hospital institution with tertiary care referral center
Methods: We reviewed our pathology database for all cases of pathologically diagnosed salivary duct carcinoma from January 1, 1995 through October 20, 2014. Patients who were outside pathology consultations and were never seen at our institution or one of its affiliates were excluded. We reviewed the electronic medical record for details regarding demographics, presentation, treatment, and outcome, including overall and disease free survival (OS and DFS). We supplemented this review with a review of our own Head and Neck Oncology Database for further clinical details.

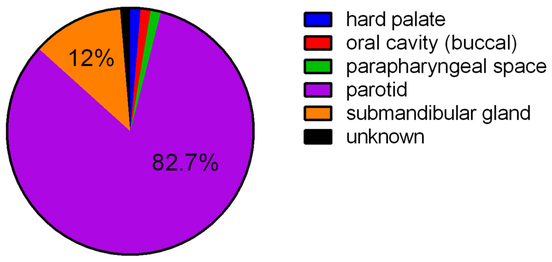
RESULTS

- 75 total cases of pathologically diagnosed salivary duct carcinoma from January 1, 1995-October 20, 2014.
- Demographics, summary data, and survival info are noted in the graphs/tables.
- Three patients (4%) had distant metastasis at the time of presentation.
- 31 patients (41.3%) had pathologic features suggestive of carcinoma ex pleomorphic adenoma.
- Rates of pathologic features were: perineural invasion (PNI) 69.3%, extracapsular spread (ECS) 57.5%, Her2+ positivity 30.7% (62% of those who were tested), vascular invasion 61.3%.
- Median OS was 3.1 year and median DFS was 2.7 years.
- Notable significant variables on univariate survival analysis (OS and/or DFS):
  - Facial nerve sacrifice (main trunk or branch) at initial parotid surgery vs. those who had dissection without sacrifice
  - Extracapsular spread (ECS)
  - Perineural invasion (PNI)
  - Vascular invasion
  - T stage
  - No association with worse OS or DFS with Her2+ positivity
- Significant decrease in OS with N2/3 stage disease
- No patients had recurrence or distant metastasis after five disease-free years.

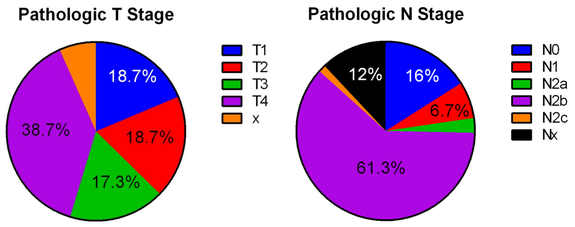
DATA ANALYSIS

Total Cases		75
Gender	Male Female	53 patients (70.7%) 22 patients (29.3%)
Average age at diagnosis	 Male Female	66 years (range 33-93) 65.3 years (33-93) 67.8 (37-84)
Smoking History	Positive Negative Unknown	43 (57.3%) 25 (33.3%) 7 (9.3%)
EtOH Use	Positive Negative Unknown	41 (54.6%) 24 (32%) 10 (13.3%)

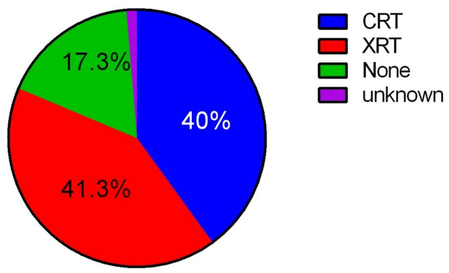
Primary Subsite



Staging

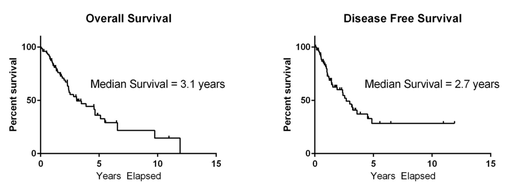


Adjuvant Therapy



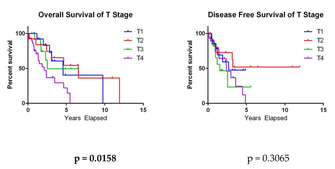
Surgery/Path Features		
Procedure	Tumor resection Biopsy only	71 (94.7%) 4 (5.3%)
Facial nerve sacrifice during parotidectomy (main trunk or branches)	Yes No	33 (55%) 27 (45%)
PNI	Yes No Unknown	52 (69.3%) 14 (18.7%) 9 (12%)
Carcinoma ex Pleomorphic Adenoma	Yes No Unknown	31 (41.3%) 42 (56%) 2 (2.7%)
ECS	Yes No Unknown	38 (57.5%) 26 (39.4%) 2 (3%)
Her2+	Positive Negative Not Tested	23 (30.7%) 14 (18.7%) 38 (50.7%)
Vascular Invasion	Yes No Not commented	46 (61.3%) 12 (16%) 17 (22.7%)

OS and DFS



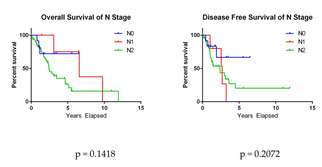
UNIVARIATE ANALYSIS

T Stage



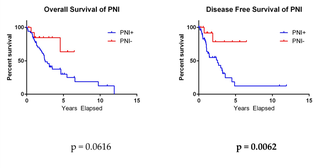
p = **0.0158** p = 0.3065

N Stage



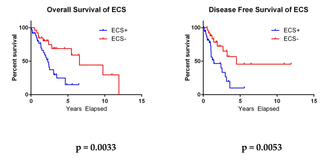
p = 0.1418 p = 0.2072

Perineural Invasion



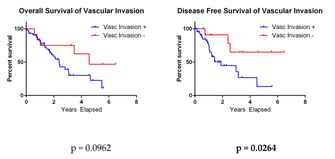
p = 0.0616 p = **0.0062**

Extracapsular Spread



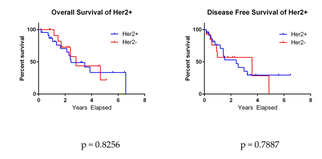
p = **0.0033** p = **0.0053**

Vascular Invasion



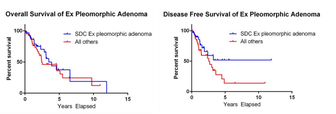
p = 0.0962 p = **0.0264**

Her2 Positivity



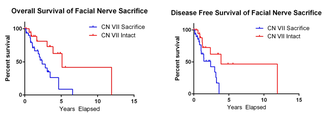
p = 0.8256 p = 0.7887

SDC ex Pleomorphic Adenoma



p = 0.4823 p = 0.0788

Facial Nerve Sacrifice



p = **0.0084** p = **0.0187**

MULTIVARIATE ANALYSIS

Multivariate analysis was performed using a Cox proportional hazards model (11 variables). Significant or nearly significant variables are shown in bold.

Overall Survival

Variable	HR (95% CI)	p-value
Age	**1.08 (1.04-1.13)**	**<0.001**
Sex, female (baseline: male)	0.81 (0.32-2.03)	0.647
Subsite submandibular gland (baseline: parotid gland)	0.26 (0.04-1.64)	0.152
Pathologic T3/4 stage (baseline: T1/2)	0.95 (0.37-2.43)	0.913
Pathologic N2/3 stage (baseline: N0/1)	**8.42 (1.84-38.50)**	**0.006**
Carcinoma ex pleomorphic adenoma (baseline: no)	1.39 (0.64-3.03)	0.410
PNI (baseline: no)	0.87 (0.12-6.01)	0.884
ECS (baseline: no)	1.66 (0.69-3.96)	0.254
Vascular invasion (baseline: no)	0.68 (0.17-2.75)	0.585
Her2 (baseline: no)	2.48 (0.73-8.47)	0.148
Facial nerve sacrifice (baseline: no)	2.70 (0.81-8.96)	0.104

Disease Free Survival

Variable	HR (95% CI)	p-value
Age	1.02 (0.97-1.06)	0.440
Sex, female (baseline: male)	**0.33 (0.11-0.96)**	**0.042**
Subsite submandibular gland (baseline: parotid gland)	**0.08 (0.01-1.12)**	**0.061**
Pathologic T3/4 stage (baseline: T1/2)	0.52 (0.17-1.62)	0.259
Pathologic N2/3 stage (baseline: N0/1)	0.71 (0.18-2.77)	0.624
Carcinoma ex pleomorphic adenoma (baseline: no)	1.18 (0.41-3.45)	0.756
PNI (baseline: no)	2.16 (0.30-15.53)	0.445
ECS (baseline: no)	2.24 (0.83-6.02)	0.111
Vascular invasion (baseline: no)	**5.30 (0.95-29.60)**	**0.057**
Her2 (baseline: no)	1.49 (0.37-6.01)	0.574
Facial nerve sacrifice (baseline: no)	**3.60 (0.91-14.25)**	**0.068**

CONCLUSIONS

- Our study of 75 patients comprises the largest single-institution review to date.
- A surprisingly large number of our cases were ex pleomorphic adenoma and had classic negative prognostic indicators such as PNI, vascular invasion, and ECS.
- Her2, previously reported as a negative prognostic indicator, was not associated with any difference in survival.
- Multivariate analysis was performed and although underpowered, was nearly significant for worse disease-free survival and/or overall survival for several indicators, including vascular invasion, higher N stage, and facial nerve sacrifice.
- The need for facial nerve sacrifice (a surrogate for gross facial nerve involvement) may indicate a more aggressive cancer with significantly worse prognosis.
- Recurrence/metastasis after five disease-free years did not occur in our study and is likely rare.

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